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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,065	03/12/2004	David Hepworth	PC25367A	8434

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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GROTON, CT 06340

EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/800,065	HEPWORTH, DAVID	
	Examiner	Art Unit	
	Janet L. Coppins	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-34* is/are pending in the application.

4a) Of the above claim(s) *28-33* is/are withdrawn from consideration.

5)☒ Claim(s) *1-13* is/are allowed.

6)☒ Claim(s) *15 and 25* is/are rejected.

7)☒ Claim(s) *16-24,26 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-13 and 15-34 are pending in the instant application.

Election/Restrictions

2. Receipt is acknowledged of Applicants' Amendment and Response, submitted September 26, 2006, which has been reviewed by the Examiner. Accordingly, claim 14 has been cancelled.

3. Applicants had previously elected Group I, drawn to compounds of formula (I) and their compositions, which appear to be allowable over the prior art. Therefore, in accordance with Rejoinder Practice and the procedures set forth in MPEP § 821.04(b), claims 15-27, directed to the process of using the allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104. Claims 28-34, directed to the invention(s) of Group IV, require all the limitations of an allowable product claim, and have NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups I-III as set forth in the Office action mailed on July 29, 2006 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15 and 25 rejected under 35 U.S.C. 112, first paragraph, as not being fully enabled. While various diseases/disorders related to the production of the NEP may be listed on pages 17-18 of the specification, the claims are not enabled for a blanket treatment method of "inhibiting NEP in a mammal" since there is no indication as to the full range of diseases or disorders that could be treated using the instant claimed process.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, the claims are directed to many diseases and conditions that are not enabled in the specification, including those encompassed by the language of claim 15 and the "laundry list" of diseases in claim 25.

The nature of the invention

The nature of the invention is of methods of treating many different diseases or

conditions that respond to the inhibition of NEP, comprising administering the instant claimed compound to a mammal in need thereof.

The state of the prior art and the predictability or lack thereof in the art

It is well recognized in the medical art that treatment of diseases or symptoms are not analogous terms. Furthermore, the diseases listed in the description on pages 17-18 of the specification are not the same but include different cancers as well as proliferative diseases and cardiovascular diseases. The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Also, in the absence of a showing of correlation between all the diseases claimed as capable of being treated by the compound of formula 1 and the inhibition of NEP, one of skill in the art is unable to fully predict possible results from the administration of the compound of formula (I).

The amount of direction or guidance present and

the presence or absence of working examples

The applicable rule is that "Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Applying this rule to claims 15 and 25, the scope of diseases claimed to be prevented or treated would thereby include all types of proliferative diseases, including diabetes and restenosis, and all types and kinds of cancer, including leukemia, and all types of cardiovascular

diseases including hypertension, atherosclerosis, hypertension, etc, inflammatory diseases such as asthma, pain, etc. Furthermore, treatment of the claimed broad range of diseases are normally disease or symptom oriented, thus are highly individualized, i.e. treating each and every disease encompassed by the claimed "metabolic diseases" would not employ the same methods. The efficacy of an individual compound against a specific disease or symptom needs to be specifically and individually supported by factual evidence. Such evidence has not been described or supported by the specification.

The Specification only describes a few *in vitro* assays of NEP inhibition, demonstrating concentrations of the claimed compounds of Formula (1) needed to suppress 50% suppression of cell proliferation (IC_{50} values), please see the Specification, pages 25-29. Given the scope of the many types of diseases/disorders included within the method claims, their varied etiologies, and the diversity of their patient populations, the disclosure in the Specification is insufficient to permit a person skilled in the art to practice a method for "inhibiting NEP in a mammal" (claim 15) without naming any specific diseases of real-world relevance. While the Applicants claim a long "laundry list" (claim 25) and cite specific diseases on pages 17-18 of the specification, including such diseases as hypertension, atherosclerosis, heart failure, glaucoma, obesity, metabolic diseases, diabetes, etc and also provide many examples of how to prepare the instantly claimed compounds, there is no indication that the compounds can treat the entire scope of all named diseases. Applicants have provided evidence that the compounds are effective for inhibiting the activity of SEP and NEP, however "the selection of the examples...used as the disclosure to support a claim must be adequately representative of the area covered by it," please see In re Cavallito et al. (CCPA 1970) 429 F2d 452, 166 USPQ 552. Therefore the specification

is enabled for certain proliferative diseases including restenosis, and atherosclerosis, and certain cardiovascular diseases, however the instant specification is lacking significant data to accommodate as many diseases as the claims are alleging by reciting the broad mechanism of "inhibiting NEP" or reciting the broad list of claim 25. The test of enablement is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. " *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214, 217-19 (CCPA 1976)).

The breadth of the claims

As noted earlier, the applicable rule is that "Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." In view of this rule, claim 15 may be reasonably interpreted to encompass atherosclerosis, restenosis, diabetes, hypertension, cirrhosis, etc and forms of cancer, as neither the claims nor the Specification expressly define a closed set of illnesses. The scope of the claim reasonably encompasses such a broad spectrum of diseases/disorders that it is unreasonable to believe, on its face, that a particular chemical compound could be used for treating so many different types, in the absence of supporting scientific data or references in the disclosure to the contrary.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art without

direction, would be unable to treat each and every disease/condition encompassed by claims 15 and 25 using the instant claimed compounds. One of skill in the art would need to determine what proliferative diseases and cancers would be benefited by the inhibiting NEP and would furthermore then have to determine whether the claimed compounds would provide treatment of all of the diseases and conditions by said activity.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of formula (I) for treating all diseases encompassed by the process of inhibiting NEP activity in claim 15. As a result, necessitating one of skill to perform an exhaustive search for which claimed diseases can be treated by the compound of formula (I) in order to practice the claimed invention of claim 25.

The Examiner suggests narrowing the scope of the diseases recited in both claims 15 and 25 to those that the Applicants are enabled for treating in the Specification, for example, "A method of inhibiting NEP in a mammal for treating FSD, FDAD, MSD, MED, atherosclerosis, hypertension, glaucoma,..." etc.

Claim Objections

6. Claims 16-24 and 26-27 are objected to as being dependent upon rejected base claims.

Conclusion

7. In conclusion, claims 1-13 and 15-34 are pending in the instant application, claims 28-33 are currently withdrawn from consideration, claims 15 and 25 are rejected, and claims 16-24 and 26-27 are objected to.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Coppins whose telephone number is 571.272.0680. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571.272.0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Coppins
December 10, 2006

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Joseph K. McKane
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